Figure 1

functionalized
microscope slide

contact printing
and covalent
attachment

Cy3 fluorophore

Cy3-R-CO₂H
2

chiral-R-acylation
region

site of
acylation

Site for acylation
with chiral Cy3 or Cy5

each spot comprises products
from one reaction, 10,800
spots per slide

10,800 simultaneous
kinetic resolutions
via acylation
with Cy3-R-CO₂H
and Cy5-S-CO₂H
DCC, DMAP

Cy5 fluorophore

Cy5-S-CO₂H
3

chiral-S-acylation
region

site of
acylation

enantiomeric ratio,
% conversion, and
absolute stereochem.
from 10,800 experiments

● = high enantiomeric ratio
● = high enantiomeric ratio
   of opposite enantiomer
□ = racemic mixture

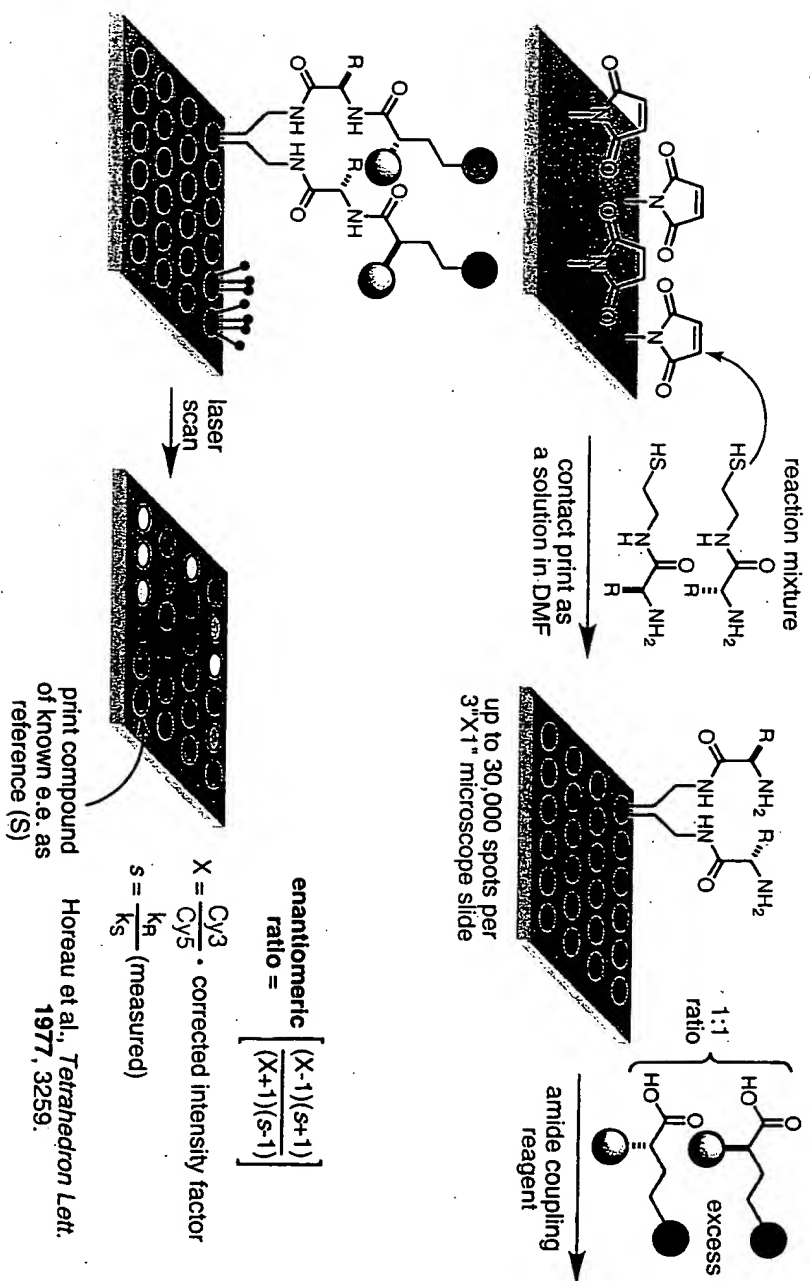$$\% \text{ conversion} = \frac{\text{absolute intensity}}{\text{intensity of known quantity}} \cdot 100$$

Figure 2

Reaction Microarrays

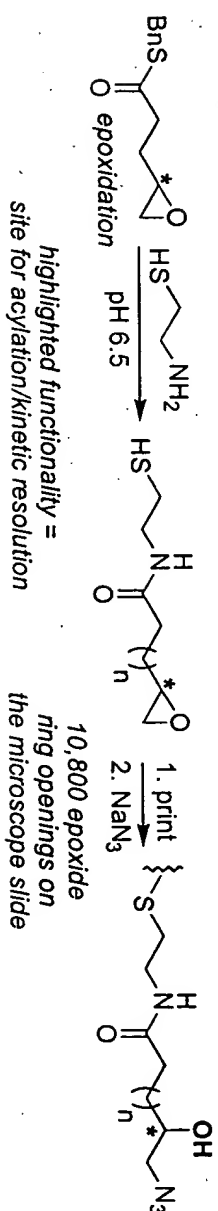reaction mixture

contact print as
a solution in DMF

laser
scan

print compound
of known e.e. as
reference (S)

up to 30,000 spots per
3"×1" microscope slide

1:1
ratio

amide coupling
reagent

excess

**enantiomeric
ratio** = $\left| \dfrac{(X-1)(s+1)}{(X+1)(s-1)} \right|$

$X = \dfrac{Cy3}{Cy5} \cdot$ corrected intensity factor

$s = \dfrac{k_R}{k_S}$ (measured)

Horeau et al., *Tetrahedron Lett.*
1977, 3259.

Figure 3

Chemical ligation as a chemoselective method of thiol incorporation for printing

Substrates for reaction microarrays

highlighted functionality =
site for acylation/kinetic resolution

10,800 epoxide
ring openings on
the microscope slide

aldol   hydroxylation   mannich   alkylation   Diels-Alder

epoxidation

Figure 4

Reagents and conditions: step 1) BocHNCH(R)CO₂H, PyAOP, ¹Pr₂NEt, DMF; step 2) Ac₂O, pyridine; step 3) 10% CF₃CO₂H and 10% Et₃SiH in CH₂Cl₂, then 3% Et₃N in CH₂Cl₂; step 4) Pentafluorophenyl diphenylphosphinate, ¹Pr₂NEt, 1:1 mixture of 1 and 2, DMF, -20 °C.
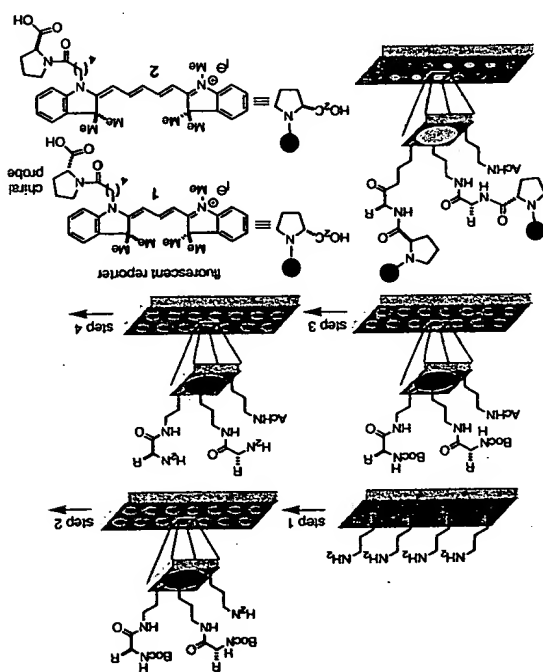
Figure 5

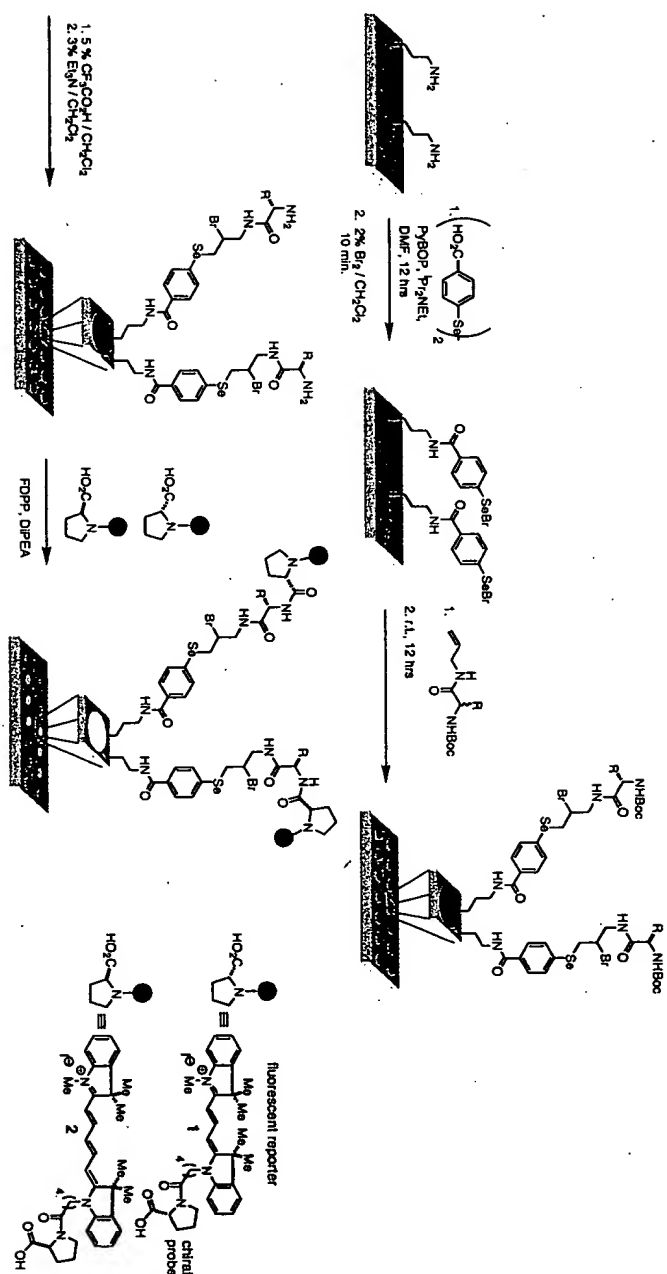Attachment of amino acids as their allyl amides to selenyl bromide-functionalized microslides
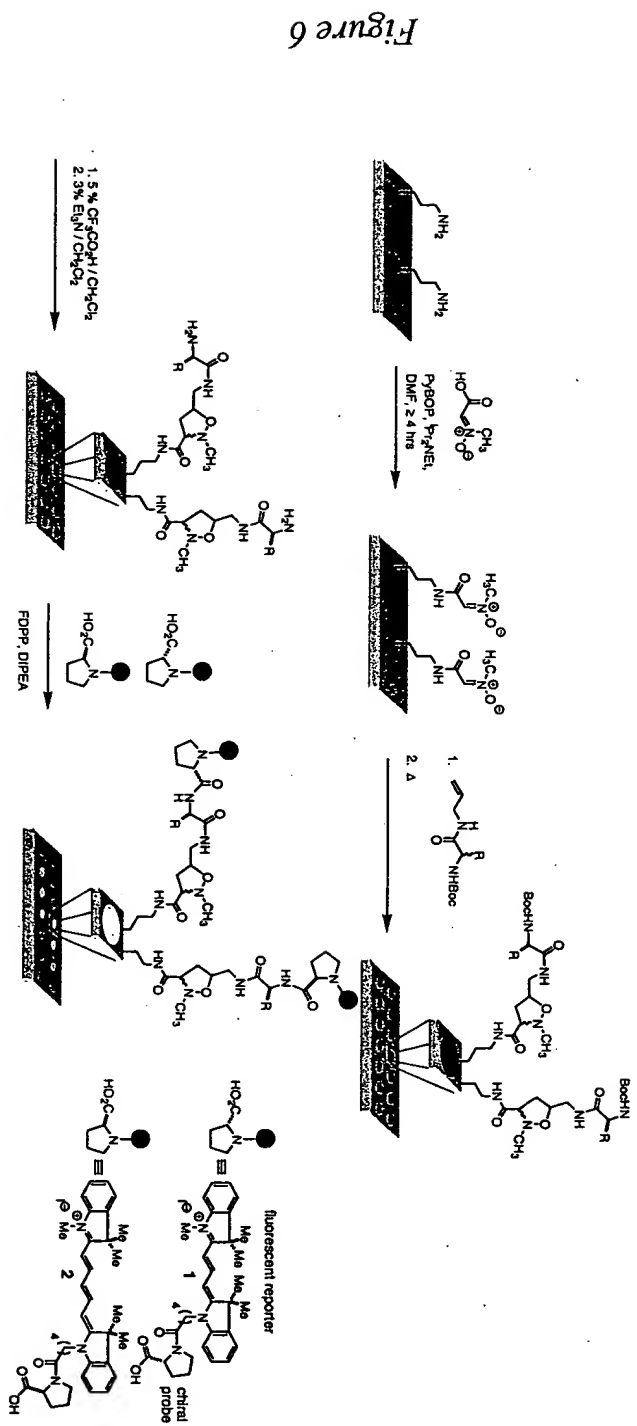
Figure 6

Attachment of amino acids as their allyl amides to nitrone-functionalized microslides

Figure 7

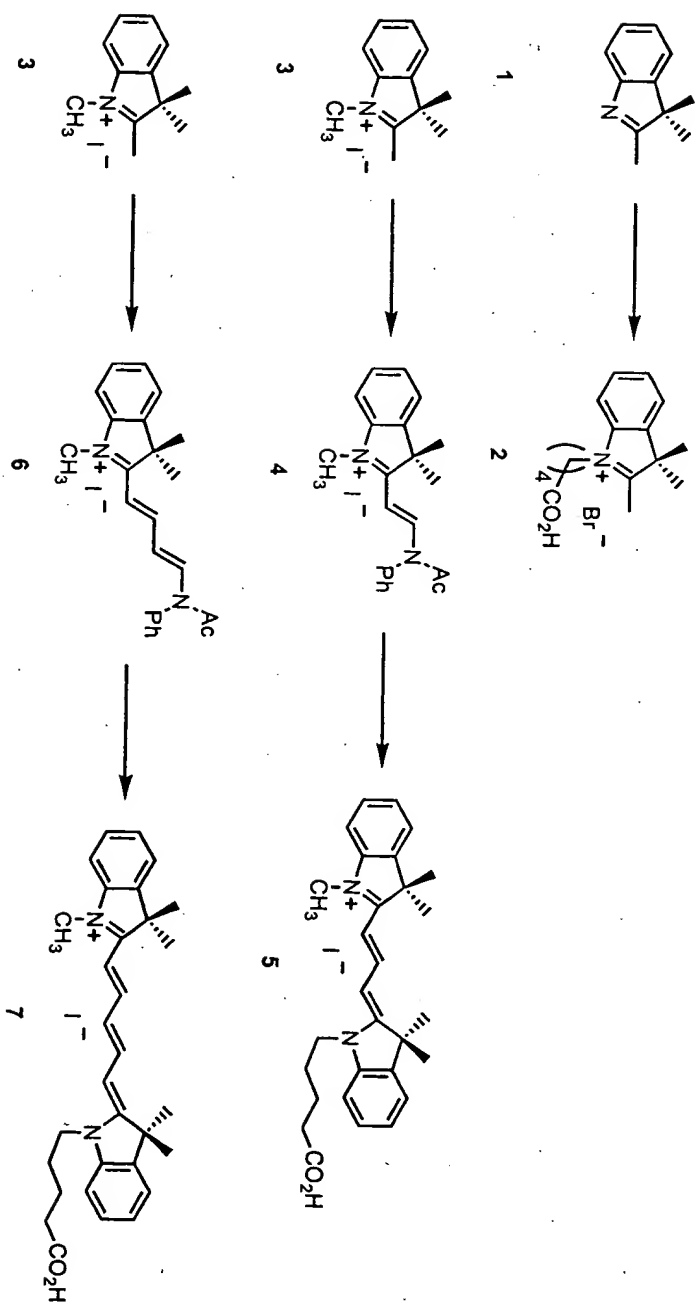Synthesis of Indocarbocyanine and Indodicarbocyanine Fluorophores

Figure 8

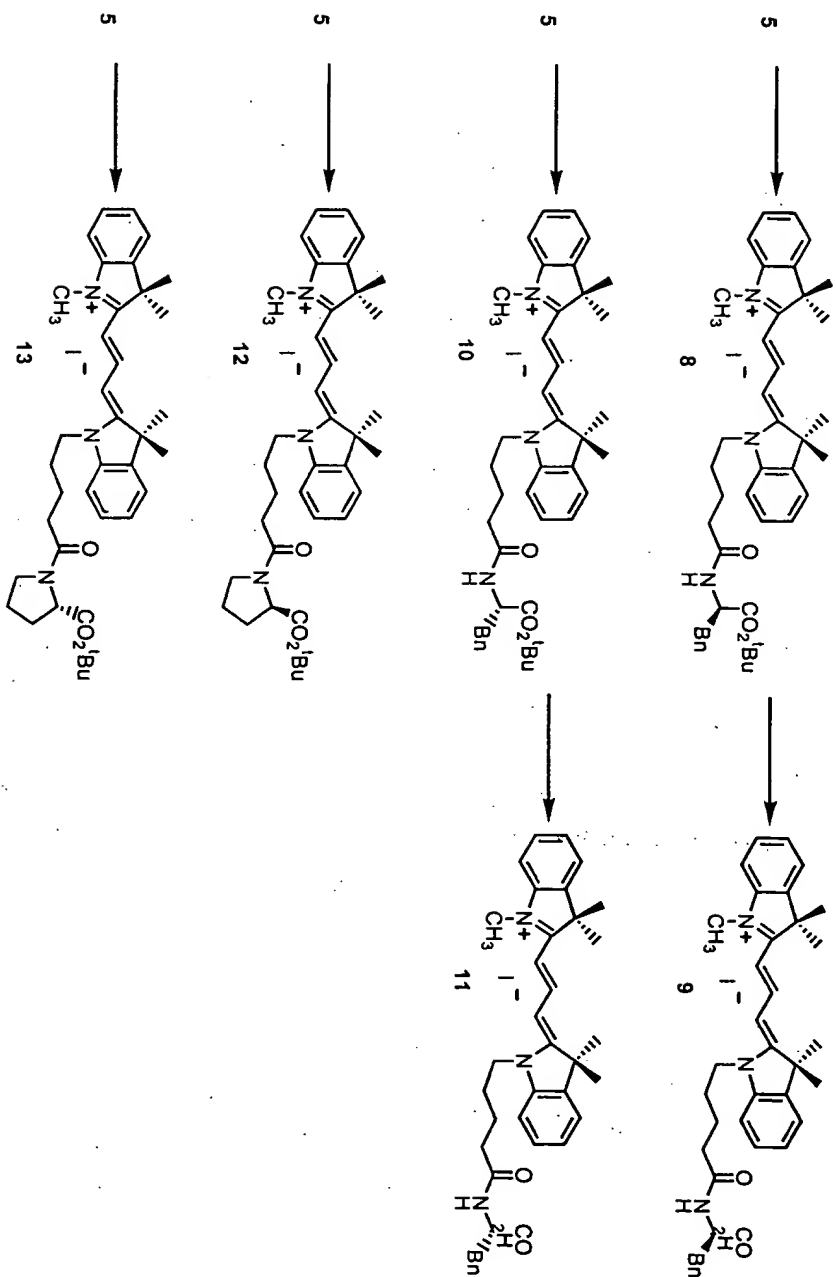Synthesis of Cy3 Fluorophore Conjugates by ^{t}Bu-Protected Amino Acids

Figure 9

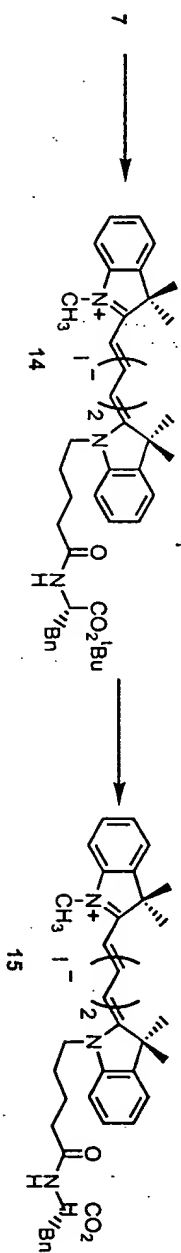Synthesis of Cy5 Fluorophore Conjugates by ᵗBu-Protected Amino Acids

Figure 10

Synthesis of Amino Acid Substrates for Printing
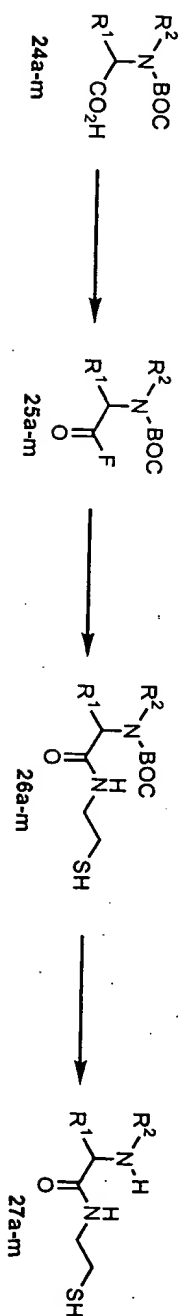
a $R^1 = R^2 = H$

(R)-b $R^1 = Me, R^2 = H$

(S)-c $R^1 = Me, R^2 = H$

(R)-d $R^1 = CH_2CH_2-, R^2 = H$

(S)-e $R^1 = CH_2CH_2-, R^2 = CH_2-$

(R)-f $R^1 = {}^iPr, R^2 = H$

(S)-g $R^1 = {}^iPr, R^2 = H$

(R)-h $R^1 = {}^iBu, R^2 = H$

(S)-i $R^1 = {}^iBu, R^2 = H$

(R)-j $R^1 = Ph, R^2 = H$

(S)-j $R^1 = Ph, R^2 = H$

(R)-k $R^1 = Ph, R^2 = H$

(S)-l $R^1 = Bn, R^2 = H$

(R)-l $R^1 = Bn, R^2 = H$

(S)-m $R^1 = Bn, R^2 = H$

Figure 11

Solid Phase Synthesis of Cyanine-Amino Acid Conjugates
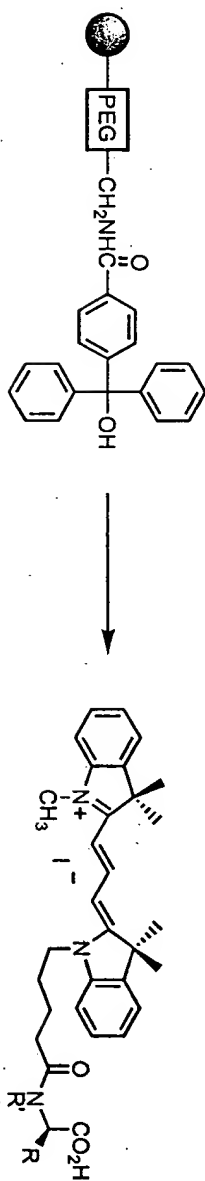
9   R = Bn, R' = H
16   R = CH₂CH₂, R' = CH₂⁻
17   R = Me, R' = H
18   R = ᶦPr, R' = H
19   R = ᶦBu, R' = H
20   R = Cyclohexylmethyl, R' = H
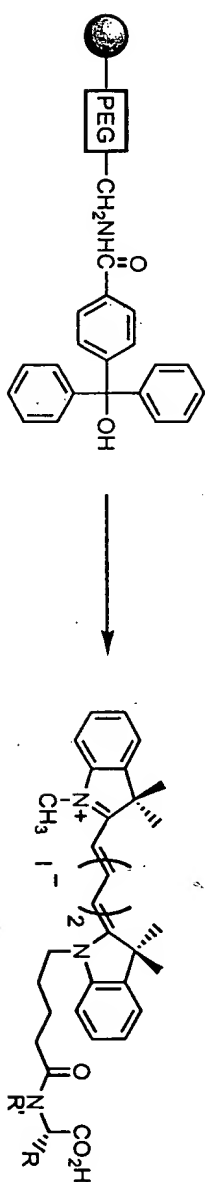
21   R = CH₂CH₂, R' = CH₂
22   R = Me, R' = H
23   R = ᶦPr, R' = H

Figure 12

Amino Acid	Approx %e.e.											
	Enantiomer D	100	80	60	40	20	0	0	20	40	60	80	100 L
Gly													
Ala													
Pro													
t-Leu													
Phg													
Phe													
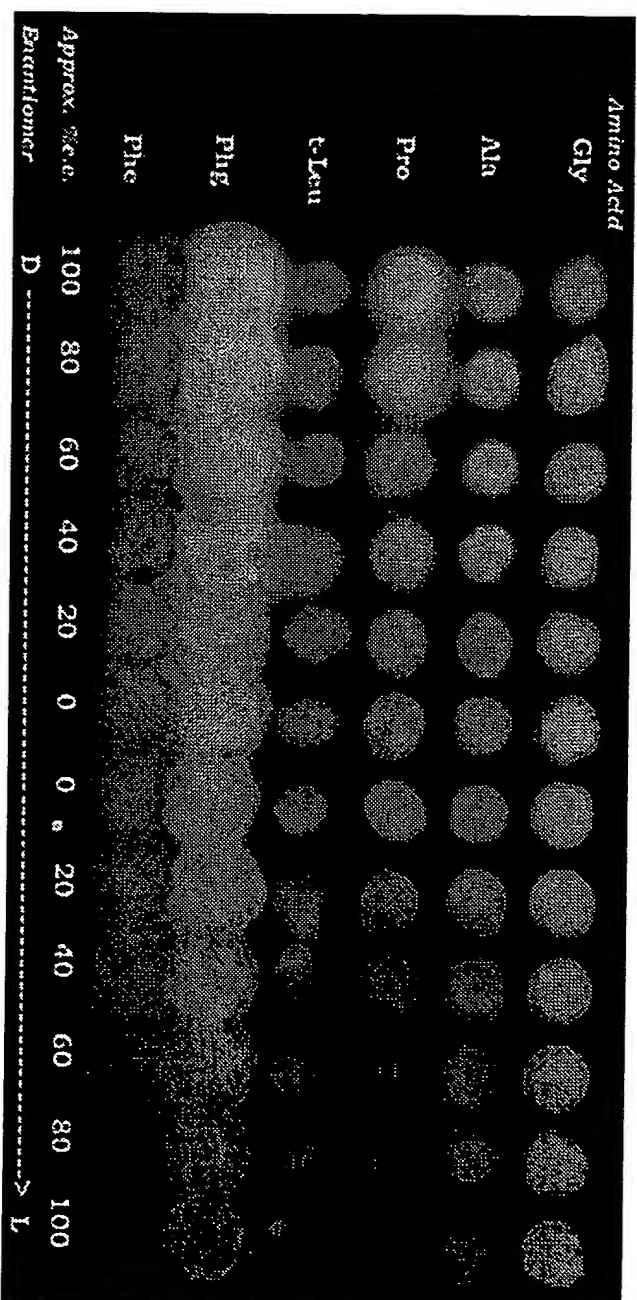
Figure 12

Ala (s = 2.0)
Calculated %e.e: 100, 87.5, 60.4, 39.7, 21.5, 7.4, 13.4, 5.2, 25.1, 49.3, 71.0, 100
Enantiomer: D, D, D, D, D, D, D, L, L, L, L, L

Pro (s = 4.7)
Calculated %e.e: 100, 87.0, 72.2, 58.3, 43.4, 31.0, 34.2, 20.1, 6.3, 12.0, 39.0, 100
Enantiomer: D, D, D, D, D, D, D, D, D, L, L, L

Phe (s = 1.8)
Calculated %e.e: 100, 85.0, 61.5, 39.6, 18.4, 0.7, 10.4, 3.4, 30.6, 53.3, 81.9, 100
Enantiomer: D, D, D, D, D, D, D, L, L, L, L, L

Figure 13

Amino Acid												
t-Leu												
t-Leu (s = 1.4)												
Approximate %e.e	100	80	60	40	20	0	0	20	40	60	80	100
Calculated %e.e	100	55.3	28.8	N/A	33.7	34.8	37.6	6.8	6.3	46.0	70.8	100
Expected enantiomer D	D	D	D	D	D	D	D	L	L	L	L	L
Enantiomer	D	D	D	N/A	D	D	D	D	L	L	L	L

Figure 14

Entry	Amino Acid	D-enantiomer ←										Actual %ee										→ L-enantiomer		Structure	Name
		100	90	80	70	60	50	40	30	20	10	0	10	20	30	40	50	60	70	80	90	100		
1	Gly																						H₂N–CO₂H	Glycine
2	Ala	100	91	80	67	63	55	50	32	21	12	0	12	24	32	42	61	60	71	76	90	100	H₃C–CO₂H	Alanine
3	Val	100	89	79		58	52	39	31	20	12	0	13	25	42	53	67	76	77	92	100		Valine	Valine
4	Leu	100	90	80	70	60	50	36	30	20	12	0	15	30	35	47	54	62	73	79	90	100	Leucine	Leucine
5	Pro	100	83	82	73	65	61	45	35	14	0	6	21	31	42	43	67	75	85	93	130		Proline	Proline
6	Ser	100	91	77	65	55	49	40	37	27	13	0	11	34	34	45	61	63	75	84	88	100	Serine	Serine
7	Cys	100	83	79	73	63	46	43	41		0		49	32	46	54	65	63	77	83	100		S-Acetamidomethyl-cysteine	S-Acetamidomethyl-cysteine

Figure 15